

New Technologies Forum 6: Rapid methods in microbiology

Report

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The sixth New Technologies Forum, on Rapid methods in microbiology (RMM), was held at the Royal Pharmaceutical Society on Thursday 6 February 2003. Twenty-five delegates attended from industry, academia, the Medicines Control Agency, and the Royal Pharmaceutical Society.

Professor Tony Moffat, Chairman of the Forum, opened the day's proceedings by welcoming those attending the Forum and providing an outline of the aims of the New Technologies Forum.

Stuart Heir (Novartis) described the current status in the US pharmaceutical industry. Although products were of high quality, there was an increasing trend towards manufacture-related defects, the efficiencies of manufacturing and Quality Assurance (QA) processes were low, innovation, modernisation and adoption of new technologies were slow, and there was a high burden on the compliance resources of the Food and Drug Administration (FDA). Using some comparisons with the automotive industry, he noted that the pharmaceutical industry had been relatively slow to adopt innovations. The standards for starting materials and products were based largely on pharmacopoeial requirements and they were often developed for older technologies. However, they formed the legal basis for approval and acceptance. The principle of testing samples was used to demonstrate compliance. There was relatively little international harmonisation.

Good Manufacturing Practice (GMP), introduced in the USA in 1962, was now applied worldwide but there were wide variations in the level of application and enforcement. GMP was based on the principle of ensuring quality by process design and controlled manufacturing conditions, and was confirmed by sample testing. Therefore, GMP required quality to be *designed and manufactured into* the product whereas current practices placed reliance on the sample testing. Testing of samples

at defined points in the manufacturing process is also used to validate the process. The Certificate of Analysis was used for release and shipment of products. The regulatory "enforcement" operates largely through the manufacturer's quality unit. Parametric release would seem to be the next logical step in the development of cGMP but experience was that it was only slowly accepted. Some recent proposals had been put forward by the European Federation of Pharmaceutical Industries and Associations (EFPIA) to widen the scope, based on extended in-process monitoring and controls. It remained to be seen whether this would be enough to gain acceptance, for example in replacing the need for a Certificate of Analysis. Overall, quality is only partly managed under the present system, in accordance with the regulatory requirements and these, together with current industry practices restrict the development of new process models and the application of new technologies. The cGMP concept requires compliance with the perceived state of the art, as established by precedents. This is exemplified by some advice on cGMP from a Parenteral Drugs Association Letter (December 2001) to always do that which is safe, prudent and good practice for your operations - "and pray you get a good reviewer and inspectors".

Experience in the use of electronic records and signatures (21 CFR Part II ¹) was informative. It fulfilled a need to define the security management of computerised systems but the industry and regulatory interpretations had extrapolated the requirements well beyond the anticipated scope, with high compliance costs. The focus by industry and regulators was on technical and legal requirements, rather than on the intended purposes. A result was that a regulation that was intended to support technological progress has in fact inhibited it.

The consequence of cGMPs was that it was difficult to anticipate the outcomes of inspections and approvals, with attendant delays in product approvals. There was also a tendency to avoid innovation (with possible regulatory delay), due to business pressures to agree to new demands to get approvals. These were all significant disincentives for new process models and technical innovations.

Concerning "risk aversion", there was increased public demand for "zero risk", backed up by litigation. Manufacturing failures and cGMP non-compliance were typically followed by more aggressive regulatory action, and calls for more enforcement. All this encourages retention of the "status quo". The standards of testing are driven by the available technology, not by the level required by the process or intended use of the product. Older technologies are seen as being "safer" than the relatively unknown new technologies.

¹ CFR: Code of Federal Regulations

However, there are some important *drivers for change*. At a global level, public expectations for personal health and access to medicines is increasing. There is reduced tolerance of poor quality or perceived risk. There are cost constraints and an increasing demand from an ageing population and public health issues (price, patent life, licensing) have political consequences.

Within the industry there were concerns that:

- sample testing and cGMP enforcement have not led to the expected levels of quality and regulatory compliance
- regulatory frameworks restrict the application of new technologies
- industry growth potential is limited by a shortage of new compounds
- the pressures on drug costs demand more effective development and production models.

The goals of process analytical technology (PAT) are to improve consistency of product quality, provide "right first time" manufacturing (to reduce costs and reduce cycle time), reduce the regulatory delays associated with changes in manufacturing, and improve the safety of chemical processes. PAT could also reduce the end-of-line laboratory testing. The challenges of introducing PAT are that it conflicts with current end-product testing, and with pharmacopoeial and other "official" test requirements. Acceptance of on-line controls and standards is slow and is in conflict to some extent with current practices in process validation. There are also legal issues.

A comparison with the automobile industry was instructive. This industry used predictive models, computerised product design and performance optimisation. Supply was "just in time" and inventories were low. Quality control of incoming materials was the responsibility of the supplier. There was continuous robotic production with on-line quality monitoring and a constant development of standards. Technological changes were rapid, were seen as positive and rapidly accepted. In contrast, the pharmaceutical industry used traditional designs, optimised by piloting experiments, and made little use of predictive models. There were extensive incoming controls, high inventories, stepwise production and low levels of automation. There was extensive on-line sampling and off-line testing in accordance with traditional standards. Process changes were very slow, seen to be associated with high risk and has slow acceptance. In summary, there were problems with both the regulators and the industry but the FDA initiative on PAT could offer great opportunities.

Stephen Denyer (University of Brighton) provided an overview of rapid microbiological techniques. Conventional microbiological methods did not allow in-

process control. Detection and counting were often separate and only culturable cells were counted. In rapid methods, other features of microorganisms were determined. Direct methods included colony formation (using biophotometry), microscopy, electronic counting and fluorescence labelling and image analysis. Indirect detection was by Adenosine tri-phosphate (ATP) luminescence, dye reduction, electrical resistance, gas production, microcalorimetry, presence of specific enzymes, analysis for cell components ("fingerprinting"), and phage technology. All the methods detected organisms and some could provide identification. However, they required large counts and were therefore generally unsuitable for relatively clean systems. The dominant systems were based on fluorescent labelling and image analysis, nucleic acid amplification, gas chromatography, and metabolic fingerprinting. In *fluorescent labelling assays*, contaminants were collected on a membrane filter and the microorganisms were stained using viability-indicating fluorophores. Detection was by fluorescent microscopy, with laser scanning to induce fluorophore excitation, and discriminatory image analysis. The method was rapid (ca 2 hours) and could be used for identification.

In *ATP bioluminescence*, microbial ATP was released which was reacted with luciferase. Luminometric analysis was performed. Membrane filter capture could be used to increase sensitivity. The method was rapid (30 min to 2 hours) and could assess viability.

In *nucleic acid amplification* cell lysis or extraction was used to release DNA, which was amplified by polymerase chain reaction (PCR), selected nucleotides were concentrated and fluorescent probes were used for quantification. Results were obtained in 1 - 3 hours and there was high sensitivity.

Gas chromatography could be used after isolation of subcultures and multi-stage extraction to release fatty acids. Comparative analysis against a database gave good identification but the method was not rapid nor sensitive.

Metabolic fingerprinting was based on the reaction of a substrate with a colour reagent, detection of the colour change and comparison with a database. Results were obtained in 4 to 18 hours and sensitivity was low.

A number of other techniques were being developed, including immunoaffinity, advanced laser scanning, and ATP amplification. Phages could be used to lyse microorganisms and the released ATP detected. Real-time detection of PCR products might soon be possible using automated homogeneous fluorescence detection systems.

Bob Johnson (Pliva) described the ChemScan methodology. The three steps involved were membrane filtration, cell labelling and laser scanning. Total viable

count was based on evidence of enzyme activity and membrane integrity. Laser scanning of the membrane revealed the presence of microorganisms and photomultiplier tube (PMT) signals were processed based on colour discrimination, signal shape and light intensity. The microscope had an automated stage and the output was a scan map. Single cell detection of bacteria, yeasts, moulds or spores was possible, results were obtained in 2 hours, results were independent of culture conditions, there was good recovery of injured, stressed and fastidious organisms, and analysis could be automated. The limitations were that the medium had to be filterable, sample preparation was highly manual, there was no identification of the microorganisms and sample preparation made further evaluation difficult.

ChemScan had been applied to the routine analysis of pharmaceutical grade water, to sterility testing, environmental monitoring and in-process control. Bob Johnson then described the application to the testing of pharmaceutical grade water and showed that the instrument and equipment controls demonstrated that ChemScan consistently met defined operational standards. Reagent and consumables controls demonstrated that false positive results would be minimal

The ChemScan method had been compared to the standard plate method for seven pure bacterial and fungal cultures. It had performed well for linearity, precision, accuracy, range and limit of detection (LOD). In equivalence testing, the ChemScan method performed better than the standard plate method in routine water monitoring. A subsequent regulatory review identified the need to perform further tests on mixed cultures and on biofilm detection. The results showed that the ChemScan method could accurately and precisely detect bacterial strains, bacterial spores, yeasts and fungi in a mixed culture. The results were equivalent to, or better than, those obtained by the standard plate method.

When ChemScan was used to detect and count organisms within biofilms from *in vivo* and *in vitro* experiments, higher counts were obtained than in the standard plate methods. It was concluded that ChemScan was a more sensitive technology.

In sterility testing, ChemScan is being evaluated for proof of technology and principle, to develop test protocols. For environmental monitoring, a new soluble microbial capture material has been developed for use in settle plates, contact surface monitoring, active air sample and swabs. Counts were similar to or higher than plate counts.

Other potential applications were testing of raw materials and products, environmental sampling, bioburden testing and biological indicators. In summary, ChemScan is the only current technology with the sensitivity and near real-time results to support in-process monitoring. It could potentially build quality into

pharmaceutical products during processing and support the ideals of PAT and parametric release.

Chris Randell (Wyeth) described the use of ATP bioluminescence. Six systems were available. The method is based on the interaction between D-luciferin (substrate), ATP (from the microorganisms) and an enzyme, luciferase, to produce emitted light that is measured. The method is primarily qualitative. It requires incubation and the cells remain viable after the test.

CELSIS "Rapiscreen" ® uses cultivation in broth for 48 hours, transfer to a cuvette and instrument-controlled end-point detection.

MILLIPORE "Microstar" ® uses membrane filtration, reaction on the surface with the spray reagent and image analysis.

PALL / GELMAN "Pallcheck" ® also uses membrane filtration and direct reading of the surface in ca 60 seconds.

HYGIENA "SystemSure" ® and BIOTRACE "CleanTrace" ®, both used to monitor hygiene, used swabs impregnated with reagents that react with ATP. Results are obtained in 30 seconds.

The methods reduce laboratory time and increase flexibility in monitoring. Some of the methods are fast and could be used for in-process monitoring.

James Bruce (Acugenics) gave an overview of the methods for the identification of microorganisms, including classical methods, those based on cellular fatty acids, utilisation of carbon sources and genetic methods.

Those based on phenotype could be quite variable. For example, fatty acid composition was dependent on temperature, culture age and growth medium. Dr Bruce then described a classification system based on phylogenic characters. This had the advantage that the sequence characteristics (based on genes coding for RNA of the small ribosomal sub-unit) are robust and are not influenced by external factors. He then described a trial to determine the accuracy and reproducibility of species determination in 18 known American type culture collection (ATCC) strains of organisms most frequently found in pharmaceutical manufacturing areas. The features of the genotypic (Microseq®, Riboprinter®) and phenotypic (Sherlock®, MicroLog®, Vitek®) identification systems were described. When used to test the strains of microorganisms, the genotypic tests performed better.

	Accuracy	Reproducibility
Microseq®	100%	100%
Riboprinter®	81%	97%
Sherlock®	50%	81%

MicroLog ®	65%	62%
Vitek ®	33%	89%

It was noted that the Vitek system used a clinical database.

A similar outcome was obtained in tests on samples of unknown organisms and in the best case only 1% of the unknowns were unidentified for genus. The methods would further improve as more organisms were characterised.

Discussion on methodologies

Paul Hargreaves (MCA) sought clarification on sensitivity of some methods. He understood that ATP detection needed 1000 cells to be present but claims were made for sensitivity to a single cell. One cell may not enter a growth phase and even if it did, it would require 5 to 55 days to grow sufficiently. The amount of DNA in a single cell was tiny.

Sensitivity was related to the volume of fluid filtered. Stephen Denyer reported that photon counting was very sensitive, down to a single organism. Long incubation periods were not necessary because spore germination was accompanied by a burst of ATP production and this could be detected.

The positive concentration ensured that cells did take up markers and no problems had been encountered in the thousands of organisms tested.

There was limited experience of comparisons of traditional and new methods run concurrently. The RMM were seen as a screen that could be integrated into a pharmaceutical process.

Paul Newby (GlaxoSmithKline) discussed the issues and barriers to the implementation of RMM. An aim must be to provide an industry context for introducing RMM, showing that RMM have an important part to play in achieving the objective under PAT. Listing the benefits, Dr Newby included significant increase in speed, increased sensitivity, the potential for in-line testing, reduction in in-process test times, and reduced potential for batch rejection and re-works.

There were technical barriers to the introduction of RMM. These included the use of test systems designed for other sectors and applications, lack of understanding by suppliers of the requirements of the pharmaceutical industry, including cGMP and validation issues, and poor documentation or guidance on equipment use. The other barriers were the conservative nature of the industry, the reluctance to move from compendial methods, uncertainty about the acceptance by regulators and a lack of managerial commitment.

Barriers to the wider use of RMM would be overcome if they were seen as part of an integrated approach to the release of products under PAT. This would involve

greater understanding and conviction in all parts of the company. The advice was to write a user specification, develop communication with regulators and be realistic about implementation and the benefits achievable.

Within GSK, non-sterile products are released on the basis of microbial limit tests, taking 5 days or more. For sterile products, sterility tests are used and these take 14 days or more. In-process testing is used for environmental monitoring, raw material testing, in-process bioburden, and water testing; the results take 4 to 5 days. These tests are potential bottlenecks and can not deliver real-time results.

The product and process requirements are paramount and the technology used must satisfy the product requirements and specifications. Selection of the technology will be guided by an understanding of the processes and the product.

The technologies of current interest to GSK were methods based on ATP bioluminescence and solid-phase laser cytometry. Implementation strategy is based on the Parenteral Drug Association (PDA) technical report 33 and the draft Pharmaceutical Forum Chapter 1223. Implementation would require an integrated approach for microbiological performance, instrument qualification, computer system compliance and education and training.

In conclusion Paul Newby pointed to the pressures on the industry, requiring new ways to increase efficiency in drug development processes. PAT will help and RMM will have an impact. However, significant technological and cultural issues must be addressed for successful implementation

Paul Hargreaves (Medicines Control Agency) considered the validation and acceptance of RMM. The theoretical basis of each test must be documented by the user and it should consider the behaviour of injured and starved cells, and spores. The experience of the LAL (*Limulus*) test was that the method took many years to be recognised but now it was accepted world wide, despite the wide variability originally found. However, the programme was driven by political pressure, the commercial interest from LAL test suppliers, cost considerations and the interest of academia in publishing scientific papers. These drivers do not apply to the RMM. The RMM used in the food industry and medical microbiology are not readily transferred to the pharmaceutical industry. New protocols are needed. These must cover the theoretical basis of the test, explore areas of potential weakness of the test and worse-case scenarios.

Validation is needed of the equipment (including computer hardware and software), the technician and the method.

Method validation should address what is being measured, what the variables are and how they are controlled. Variables include the source of the material and prior

treatment or storage conditions. It is important to be clear about whether the method differentiates between viable, non-culturable and dead cells. The results from RMM will almost certainly differ from those with conventional methods and a decision is needed on how these differences will be handled. A number of pathogens are not culturable but could be detected by RMM, thereby improving the quality of medicinal products by detecting organisms not previously detected. Other examples of non-culturability of viable cells are known and this may be influenced by treatment of the cells. Some RMM can differentiate between viable and non-culturable cells, whereas others may not.

In conclusion, Paul Hargreaves said that RMM should be encouraged but suitability should be subjected to rigorous scientific assessment, with published peer-reviewed papers. Equipment manufacturers' claims and literature were not acceptable substitutes. RMM may provide enhanced safety, particularly for immunocompromised patients. Qualified microbiologists were needed to understand the basis of the tests.

Bryan Riley (Food and Drug Administration) noted that the FDA had not received applications for the use of RMM for release tests, such as microbial limits and sterility tests. The regulatory concerns were about the increased sensitivity of RMM, with the potential to change (raise) the microbial limit acceptance criteria, and the occurrence of “false positives” in sterility tests.

Dr Riley stated that the FDA would be willing to allow applicants to raise microbial limits acceptance criteria, to allow for the increased sensitivity of RMM, with the proper scientific justification.

The FDA initiatives to facilitate the use of RMM by the pharmaceutical industry were: the use of PAT (including RMM), the establishment of a Microbiology Subcommittee for the Advisory Committee for Pharmaceutical Science (ACPS), and updating of cGMP through the use of product specialists for inspections and inspection dispute resolution at the Centre level.

In summary, Bryan Riley said that there was a need for comparisons between RMM and traditional methods, and asked why the industry was apprehensive about the introduction of RMM. Dr Riley also encouraged industry to meet with the FDA to discuss the scientific and regulatory issues concerning the use of RMM in their manufacturing processes.

General Discussion

Tony Moffat invited the Forum to consider how to move forward with getting rapid methods more widely used. As in previous Forums, the regulators were waiting for

the submissions with the new methods. Paul Newby had identified some barriers and these should now be examined.

There was agreement that the "old" technologies were not very good but the new technologies gave different answers. There were sound scientific reasons for this difference, including the "recovery period" for damaged microorganisms. One concern was whether use of the new methodology would raise the criteria of acceptance, without an increase in standards of safety.

There was an absence of peer review scientific papers on rapid methods. Such papers could help to establish the techniques. Academia had contributed to the science basis of the tests but there was a gap in the research funding because research councils would not fund methods application research.

Tony Moffat reported on the funding of near infrared (NIR) research by the Pharmaceutical Analytical Sciences Group, a consortium of ca 24 companies. This could be a useful model (although PASG does not have a microbiology arm). A view from one pharmaceutical company was that an individual company would not fund research into the commercial test systems, but might do so as a consortium. Although the PAT initiative had originated in Europe, the FDA was to be congratulated for taking PAT forward.

The introduction of new technologies had to be driven by manufacturing, not by R & D, and this was starting to happen.

Another impediment arose because of the myth that existing microbiological test processes were validated. Processes were not validated but this could change as the new analytical techniques became available to provide physical measurements of the processes.

Kirsty Wills noted that a number of the RMM are used successfully² and advocated that these successes should be publicised through the regulators. Any further advances in the instrument design would only follow the more widespread use of the methods.

Stewart Green reported that Wyeth had experienced no big barriers to the introduction of RMM. The microbiologists had noted that analytical colleagues successfully got their techniques through and had drawn on the experience. Now, only 2.6 % of applications used traditional microbiological methods.

² Note: It was reported that there were two approvals for Chemunex Scan RDI. One was in the UK (GSK, for process water) and one in Spain. There were also approvals in many countries for the use of Celsis RapiScreen for a wide range of non-sterile products from a number of manufacturers.

To some extent the methods being discussed were chemical methods based on the characteristics of microbes.

A major impediment was seen to be the resistance of registration departments in some pharmaceutical companies to change. Missed submission deadlines were "unacceptable" to registration departments and the introduction of new technologies was seen as a likely cause for delay, with huge attendant losses in revenue from sales. One solution was to introduce the new technology as a variation for an established product, and not on a new chemical entity. The US FDA system allowed this to be done via a "prior approval supplement" for a significant regulatory change. In Europe, it would be necessary to proceed via each individual country and companies would not do this. The experience at Wyeth was that the turn-around time for the MCA was very good but other European national regulatory authorities gave varied approval times.

MCA inspectors would look at any variation, identify questions to be addressed to the company, and then discuss how these would be resolved.

On the effect on the Medicines Testing Scheme, Andy Charvill reported that microbiological work was out-sourced. However, the techniques under discussion were chemistry-based and so should go through the regulatory process relatively easily. In contrast, it was pointed out that although this should be true, the standards being applied to the new techniques are much higher than being applied to existing techniques and this favours staying with the older techniques. There was a need to understand the reasons for the differences.

Experience had shown that the new methods gave "any answer you wanted", with great discrepancies between the methods. The results also differed greatly from those obtained with the older methods and assessors accepted that the measured bioburden would change with the test method used. This did not mean that the product was any less safe.

Concerning the inclusion of new methods in pharmacopoeias, this would not occur until the methods were "generic" and used by more than one company. Nevertheless, draft monographs were being developed. It was pointed out that if a method was introduced in a pharmacopoeia monograph and the method was introduced into the process within 6 months then no variation was needed. However, it was reported that this arrangement would cease in July 2003

In further discussions on the role of registration departments, the good experience of Wyeth was cited. Within the company, there was a champion at a high level and this had ensured that registration and validation departments worked closely with the manufacturing departments. It was reported that AstraZeneca recognised this problem and there were internal discussions in progress.

Dianne Lee considered that the role of the registration departments included providing advice on registration and encouraging a dialogue with the regulators. She undertook to take the message back to the British Institute of Regulatory Affairs (BIRA), and to see if an editorial on this could be included in a future edition of the BIRA and the European Society of Regulatory Affairs (ESRA) journals.

A question arose about potential interference of test results from formulation factors. These were looked at during development. Preservatives were recognised to cause problems in both old and new tests.

The experience of equipment manufacturers was that the new tests were very widely used in other industries (such as cosmetics) where there were no regulatory barriers to overcome.

Dr Chatterjee (MCA), speaking from the perspective of an assessor of pharmaceutical variations, noted that registration departments were intended as a bulwark against the submission of poor applications. It was possible that companies might consult their insurers on risks associated with variations.

Summing up

Kirsty Wills (consultant) reported that a research project had established that some of the questions raised in the Forum had been raised by potential users of RMM. The level of adoption in the US was substantially lower than in Europe, although there was a high level of interest there. The principal concerns were over the regulations and validation of the methodologies used. About 60% of those surveyed had evaluated RMM. Only 27% had adopted the methodologies, although 41% had plans to do so. Nevertheless, there were reported to be two approvals granted by MCA and EMEA for tests using Chemunex equipment.

It was evident that much progress had been made since 1997 and there were many users of RMM. She advocated that the hurdles for the new tests not be set too high, particularly where the new tests were demonstrably better than the old tests. There were still some issues about the technologies and the scientific basis was not always fully understood at present. If the current tests were used more widely, the equipment manufacturers would continue to invest in further development of the equipment.

The view was that there was a clear need to establish a higher status for microbiologists working in the pharmaceutical industry.

There should be more work undertaken with the pharmacopoeias so that the technologies were defined in the specifications.

There was a clear need to overcome hurdles in the industry's registration departments, as identified in the Forum and this could only be achieved through discussion and education.

The best route to getting the methodologies established appeared to be through licence variations. It had been reported that one CPMP variation had successfully proceeded through the EMEA. It was likely that the first submission to the FDA would go from a European site. There was clearly a lot of experience of the use of RMM but this was not visible to the regulatory authorities as it did not appear in marketing applications. It now needed the last step to get the technologies established as method for use in applications.

EXECUTIVE SUMMARY

The Forum identified the following points

1. Rapid microbiological methods (RMM) offer substantial advantages over conventional methods for speed of the tests and should be an integral part of PAT and process understanding.
2. The regulatory authorities seek to encourage the adoption of RMM by the industry.
3. Companies would need to establish validation packages and should not rely solely on the literature provided by suppliers. The methods should be tested under the various conditions that are likely to be encountered in practice, to assess for robustness.
4. The reasons for the differences in results of RMM, compared to conventional methods, should be addressed and the acceptance criteria should be set accordingly.
5. More academic research on RMM should be encouraged. The outcome of successful applications of RMM should be publicised more widely.
6. Equipment suppliers would invest in the development of the next generation of equipment only when it becomes evident that the technology was being taken up by the industry.
7. The RMM should be considered for inclusion as compendial methods.

Persons attending were Dr Ros Baird (University of Bath), Dr Jim Bruce (Acugenics), Elizabeth Castles (Medicines Control Agency), Andy Charvill (Medicines Control Agency), Richard Chatterjee (Medicines Control Agency), Dr John Clements (Royal Pharmaceutical Society), Professor Stephen Denyer (University of Brighton), Kia Frenssen (AstraZeneca), Stewart Green (Wyeth), Dr Roger Guest (GSK), Paul Hargreaves (Medicines Control Agency), Dr Stuart Heir (Novartis), Dr Robert Johnson (GSK), Dianne Lee (BIRA), Dr Mike Lee (Pfizer), Ken Leiper (Benson Associates), Professor Tony Moffat (Royal Pharmaceutical Society, Chairman), Dr Fiona Mortimor (Medicines Control Agency), Dr Paul Newby (GSK), Dr Rosemary Pask-Hughes (BP Secretariat), Dr Keith Pugh (Medicines Control Agency), Chris Randell (Wyeth), Brain Riley (Food and Drug Administration), Matilda Vallendar (BP Secretariat) and Dr Kirsty Wills (Consultant).

Apologies were received from Dr Roger Alexander (Medicines Control Agency), Mr Paul Graham (MSD) and Dr Steve Wicks (Pfizer)

The New Technologies Forum was established by the Royal Pharmaceutical Society in 1998. The purpose of each Forum is to bring together representatives of the pharmaceutical industry and the Medicines Control Agency to discuss new technologies that are being, or may soon be, used in seeking a Marketing Authorisation for a new medicine.

Those with views on the Forum, or with suggestions for areas to be included (with reasons and priorities) are invited to write to Professor Tony Moffat, Chief Scientist, Royal Pharmaceutical Society of Great Britain, 1 Lambeth High Street, London SE1 7JN (Tel: 0207 735 9141 Fax: 0207 820 3918. E-mail: tmoffat@rpsgb.org.uk)

The Steering Group is

Professor Tony Moffat (Royal Pharmaceutical Society, Chairman)

Dr Roger Alexander (Medicines Control Agency)

Dr John Clements (Royal Pharmaceutical Society, Science Secretary)

Mr Paul Graham (MSD and representing PASG)

Dr Roger Guest (GlaxoSmithKline)

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Mr Ken Leiper (Benson Associates)

Dr Keith Pugh (Medicines Control Agency)

Dr Steve Wicks (Pfizer)

More details about the New Technologies Forum are to be found on the Royal Pharmaceutical Society's Homepage at: www.rpsgb.org.uk

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